Office Action Summary	Application No.	Applicant(s)	
	09/910,388	KUNZ, LAWRENCE L.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50,52-55,58 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50,52-55,58 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/7/10*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20100312*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection or objection not reiterated in this Action is withdrawn.

Status of the claims

As noted on the attached interview summary, claim 55 remains pending.

Claim Rejections - 35 USC § 103

Claims 50, 52-55, 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over March et al. (US 5,171,217, of record), Khan et al. (US 5,413,797, of record), Baker (US 4,919,939, of record), Shaw (US 4,233,968, of record) and Haugwitz et al. (US 4,942,184, of record).

The claims are directed to methods of reducing restenosis following a vascular surgical procedure comprising locally administering a biocompatible, non-biodegradable sustained release dosage form comprising a therapeutic agent in an amount that inhibits a vascular smooth muscle cell activity without killing the cell. In specific embodiments the surgical procedure is stent placement or angioplasty, the administration is direct to vascular smooth muscle tissue and occurs during or after the procedure, the agent is taxol or taxotere and the dosage form is a microparticle.

March et al. teach (see columns 1-3) that studies have indicated that angioplasty may produce endothelial denudation, injury to the vascular wall and rupture of the vasa vasorum, and that the accompanying uncontrolled proliferation of smooth muscle cells

within the arterial wall has been widely implicated as a prominent factor in the resulting restenosis. March et al. teach methods and compositions for delivering a drug to an affected intramural site for sustained release in conjunction with procedures such as angioplasty or stent placement. The drug is carried by microparticles of a physiologically-compatible, biodegradable polymer and injected under directed pressure into the wall of a body vessel in the region of the affected site. March et al. teach that administration of a smooth muscle cell inhibitor may precede, attend or follow angioplasty. Delivery can be by catheter or other injection device. One particular class of therapeutic agents taught by March et al. is anti-mitotic agents.

March et al. do not teach non-biodegradable polymers in their sustained-release compositions, but at the time the invention was made it was well known to those of ordinary skill in the art that both biodegradable and non-biodegradable polymers were routinely used in such dosage forms. This concept is illustrated by the teachings of Baker, Shaw and Khan et al., who each teach polymeric drug compositions where the polymer can be either biodegradable or non-biodegradable. Khan et al. further teach at column 1, lines 54-64 that one way of controlling blood levels of a compound is to administer it in the form of a polymeric matrix that releases compound as a function of polymer degradation and/or drug diffusion and that both biodegradable and non-biodegradable polymers have been used for such compositions. The release is controlled by selection of the appropriate polymer, encapsulation conditions, and drug loading and excipients.

Haugwitz et al. teach that taxol is an anti-mitotic compound (see column 1, lines 14-30).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce the sustained release compositions taught by March et al. as suitable for treatment of restenosis following angioplasty or stent placement using a non-biodegradable polymer. One of ordinary skill in the art would recognize that use of a non-biodegradable polymer in place of a biodegradable polymer is a matter of design choice because those in the art were aware based on the teachings of Shaw, Baker and Khan that these types of polymers were routinely used interchangeably in drug delivery formulations. It would further have been obvious to use taxol as the therapeutic agent in the method of March et al. because March et al. explicitly teach that anti-mitotic agents are a suitable class of agents and Haugwitz et al. teach that taxol is an anti-mitotic agent. The use of a cytostatic amount of taxol that does not kill cells is a matter of routine optimization of dosage. See MPEP 2144.05 II: "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Thus, the invention of claims 50, 52-55, 58 and 59 would have been obvious, as a whole, at the time the invention was made.

Response to Arguments

Applicants argue the cited references do not disclose or suggest the claimed subject matter, arguing that March does not disclose or suggest the claimed therapeutic agents or local administration of a cytostatic amount of a therapeutic agent that inhibits a vascular smooth muscle cell activity without killing the cell. Applicants further assert

Khan, Baker, Shaw, or Haugwitz do not cure this deficiency and enumerate the individual teachings of these references. Applicants note Baker is wholly unrelated to inhibition of smooth muscle cells and Haugwitz focuses on the cytotoxic uses for taxol.

These arguments are not persuasive because it is not required that March teach the claimed agents and the use of a cytostatic amount. The rejection is based on the teachings of all the cited references, not March alone. The claimed therapeutic agents are suggested by the teaching of March that anti-mitotic agents are a suitable therapeutic. Those in the art recognize (based on the teachings of Haugwitz) that taxol is an anti-mitotic agent. Use of an amount of therapeutic that does not kill cells would be (as noted in the rejection) a matter of routine optimization of dosages.

Applicants argue a person of ordinary skill in the art would not look to Khan, Baker, Shaw, and Haugwitz to satisfy March's deficiency, because they are wholly unrelated to the claimed methods of reducing restenosis.

This argument is not persuasive because Khan, Baker, Shaw and Haugwitz were not cited to teach reduction of restenosis, but as evidence that those of ordinary skill recognize that both biodegradable and non-biodegradable polymers were routinely used in sustained-release compositions.

Applicants further argue even if the cited references were combined the resulting method would not be that claimed because the resulting method still would not require locally administering a cytostatic amount of a therapeutic agent that inhibits a vascular smooth muscle cell activity without killing the cell.

This argument is not persuasive because, as noted in the rejection, use of a cytostatic amount of taxol that does not kill cells is a matter of routine optimization of dosage.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi, can be reached on 571-272-3311. The central FAX Number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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